

Prostate Cancer in the Elderly Patient: Who Qualifies for Treatment?



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Introduction

Prostate cancer (PCa) is the most common cancer in men and the second most common cause of cancer death with increasing incidence and prevalence during aging [1]. Due to demographic changes and increasing longevity, more and more men are confronted with this disease and its consequences. It is very important to understand, that prostate cancer morbidity is a much more relevant problem than it is actual mortality. Many more men suffer from complications of the disease (i.e. outflow obstruction of the upper and lower urinary tract, hematuria, bone metastases with pain, pathological fractures and spinal cord infiltration) or the adverse effects of treatments than men who ultimately die from it [2]. Hence, with higher age, the loss of quality of life is increasingly more important than the loss of quantity of life. Overall, it is a growing medical and socio-economical problem. Specific treatment algorithms for elderly men with PCa must be established. Even some elderly patients may benefit from active treatment, however, a very careful patient selection must be performed in this subpopulation to avoid over- as well as under treatment [3]. Patient characteristics as well as tumor biology must be taken into account in order to tailor the treatment.

Assessment of the Elderly Patients Risk Profile

In clinical practice, there remain the difficult question: which patient can profit from active treatment, respectively and at least as important, which patient will see more harm than benefit from treatment? Whereas it is relatively easy to assess and categorize the aggressiveness of the cancer [4], it is much more challenging doing the same for the patient. Unfortunately, there exist no easily applicable triage tools for such an assessment and to guide ultimately treatment decisions in these patients. Chronological age alone is often not sufficient and clinical gut feeling concerning the biology of the patient can be very misleading. Nevertheless, in terms of practicability and as a very rough pattern, patient's ≥ 75 years can be taken as the target population keeping clearly in mind, that this population is much more heterogeneous than younger populations. Hence,

whenever treatment comes into discussion in elderly patients an assessment of the patient's biology and life expectancy should be performed.

A multidimensional geriatric assessment including functionality and mobility, psyche and cognition, co-morbidity as well as social and nutritional status is of great help [3]. Today, there exists valuable and valid assessment instruments helping to uncover primarily unrecognized deficiencies [5,6] and to graduate elderly patients into risk-groups (fit; limited; frail) [3]. Of course, the assessment is a time consuming process and exceeds the resources in the daily practice. Further and mainly, the interpretation of findings in the clinical context should be left in the hands of the corresponding experts, the geriatric colleagues. Whereas fit patients with a life expectancy of over 10 years can benefit for treatments comparable to younger patients, frail patients with very limited life expectancy will hardly benefit of aggressive treatment since adverse events surpasses in most cases the potential benefits. The Society of Geriatric Oncology Prostate Cancer Working Group published recently their corresponding recommendations [7].

How to Proceed in Clinical Practice?

Elderly, asymptomatic patients without the diagnosis of prostate cancer should not be screened for the disease, since the probability detecting insignificant PCa is very high. However, if patients suffer from symptoms like urinary outflow retention, hematuria, skeletal pain or unclear reduction of the general state of health, the potential presence of PCa is underlying cause for the bother should be considered. According to an autopsy study in the US, the occult prevalence of prostate cancer in the age of 71-80 years reaches 83% [8], hence, diagnosis should be confirmed or ruled out beginning with PSA test, DRE and in case of increased suspicion, prostate biopsy and imaging, respectively.

In case of localized PCa the indication for a local treatment in curative intent must be placed with special reservation. If at all, only fit patients with a life expectancy of over 10 years and

aggressive PCa do qualify. In all other cases, treatment intention should be symptom oriented; PSA monitoring in intermediate to high risk PCa however is indicated so to not miss progression into metastasized stage.

In case of metastasized PCa, actually all patients from fit to frail can benefit from palliative treatment. Importantly, pure PSA manipulation should be avoided and indication for the initiation of a treatment would be proven osseous metastases or symptomatic progression. However, also in here, the aggressiveness must be tailored to the individual patient. First line treatment would be, like in younger patients, androgen deprivation therapy (ADT) [7]. It should be considered that this treatment is associated with higher risk of osteoporosis, metabolic syndrome and cardiovascular events especially in elderly patients [9], hence, an anti-reabsorbing therapy with Denosumab as well as supplementation of calcium and vitamin D3 should be established. Recently, it could have been shown in a phase III trial, that an early systemic therapy during the hormone sensitive phase of PCa with docetaxel in combination with ADT can improve survival substantially and that elderly men with good performance status can benefit as much as younger men [10], especially in case of high tumor burden. On the other side, frail patient will not benefit since adverse effect of treatment will outweigh potential benefits. In case of castration-resistant PCa it has been shown that also elderly patients can benefit from advanced systemic therapy (chemotherapy or advanced hormonal manipulation) [11-15], however, the consideration of the overall situation and the risk profile of the patient becomes increasingly important. Additionally, in this situation a discussion of principles, optimally in presence of the patient and his relatives at the latest should be performed to clarify the goals and to give a realistic summary of the possible and clinical meaningful therapy-options in the future. It is on an individual but also socio-economic point of view very important, to remove unrealistic ideas and to organize symptom oriented palliative treatment in and at the right time.

Conclusion

The prevalence of PCa in elderly men is very high. The appearance of the disease is diverse and reaches from asymptomatic and unrecognized up to aggressive and life threatening. Also elderly man can benefit from treatment, in very selected patients even in case of localized disease, in most patients in case of metastasized disease. However, since the population of elderly men is heterogeneous any attempt of treatment must be considered carefully with the goal to avoid over- but also under-treatment. The very high rate of morbidity of the disease must be kept seriously in mind, since complications of PCa and its associated loss in quality of life weights for most elderly men more than loss in quantity of life. A geriatric assessment is of great value in almost all cases

to tailor treatment aggressiveness in accordance to the patient's individual risk profile. At the latest, in case of castration resistant PCa unrealistic goals of advanced treatment options must be removed and symptom-oriented palliative treatment organized in and at the right time.

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